

Suppression of Diagonal Peaks with Singular Value Decomposition

Guang Zhu,¹ Wing Y. Choy, Guoqiang Song, and B. C. Sanctuary

Department of Biochemistry, Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong

Received July 28, 1997; revised February 6, 1998

A number of modified two-dimensional NMR pulse sequences have been developed to suppress the diagonal peaks which may introduce severe spectral distortions, such as t_1 -ridges and large dispersive signals on the diagonal. However, these modifications increase the minimum number of scans, require more complicated experimental designs, and often decrease the sensitivity of the experiment. Here we present a post-acquisition method to remove the undesirable diagonal peaks by using singular value decomposition based on the observation that the diagonal peaks are larger in amplitude than the off-diagonal peaks. The effectiveness of the scheme is demonstrated by applying the method to process a phase sensitive COSY spectrum of alkyl-cyclohexyleneacetic ester. The method can also be used for the removal of the diagonal peaks in NOESY, ROESY, and other correlation spectra. © 1998 Academic Press

Two-dimensional (2D) NMR spectroscopy is a well-established technique for acquiring information on the structure and function of molecules. Among the many 2D NMR experiments, the COSY experiment is particularly useful in identifying networks of scalar-coupled spins (1, 2). A number of modified COSY pulse sequences, such as adding a double quantum filter, have been developed to obtain pure phased spectra and to suppress diagonal peaks (3–5). However, these modifications increase the minimum number of scans needed, require more complicated experimental designs, and often decrease the sensitivity of the experiment. These diagonal peaks often have a 90° phase difference to the off-diagonal signals and distort the spectrum, making the analysis of this type of spectrum difficult. In addition to the experimental modifications, several post-acquisition methods have been proposed to remove unwanted diagonal peaks based on digital filtering (6–8) or a combination of removing absorptive diagonal peaks and Hilbert transformation (9, 10).

We report an alternative numerical method that can be used to eliminate the undesirable diagonal peaks by the singular value decomposition (SVD) scheme based on the observation that diagonal peaks commonly have a much larger amplitude than the off-diagonal peaks (11). One could also apply the Karhunen transformation to achieve the same goal (12). The SVD procedure described here involves calculating the singular values of Toeplitz matrices formed from the

FIDs in the indirectly detected (t_1) domain after the Fourier transformation of the directly detected (t_2) domain. These FIDs are reconstructed following the removal of the largest singular values. The final spectrum which is free of the dispersive resonances can be obtained by Fourier transformation of the t_1 domain. We demonstrate here that pure-phase COSY spectra with the suppression of diagonal peaks can readily be obtained by the use of this proposed method, as is described below.

A 1D FID, $\{x_n | n = 1, \dots, N\}$, is composed of the summation of exponentially damped sinusoids. A forward Toeplitz matrix \mathbf{T} , as in the forward linear prediction method (13), can be formed as

$$\mathbf{T} = \begin{bmatrix} x_1 & x_2 & \cdots & x_M \\ x_2 & x_3 & \cdots & x_{M+1} \\ \cdot & \cdot & \cdots & \cdot \\ x_{N-M+1} & x_{N-M+2} & \cdots & x_N \end{bmatrix}, \quad [1]$$

where N is the number of data points in the 1D FID, and M is the window size of the Toeplitz matrix. According to the SVD principle (14), an $(N - M) \times M$ matrix \mathbf{T} can be expressed as the product of an $(N - M) \times (N - M)$ unitary matrix \mathbf{U} , an $(N - M) \times M$ diagonal matrix Σ , and an $M \times M$ unitary matrix \mathbf{V} according to

$$\mathbf{T} = \mathbf{U}\Sigma\mathbf{V}^+, \quad [2]$$

where $^+$ denotes the conjugate transpose. The diagonal elements, σ_i , of the matrix Σ are positive and its off-diagonal elements are zero. Furthermore, the largest component, σ_1 , corresponds to the largest sinusoid component in the 1D FID. A new 1D FID from the indirectly detected domain which is free of the diagonal peak can be created from the Toeplitz matrix \mathbf{T}' following Eq. [2] by zeroing the largest singular value and constructing a new Toeplitz matrix \mathbf{T}' in the following manner,

$$\mathbf{T}' = \mathbf{U}\Sigma'\mathbf{V}^+, \quad [3]$$

where Σ' is the matrix Σ with $\sigma_1 = 0$ and the rest of the elements are unchanged. The spectrum obtained from Fou-

¹ To whom correspondence should be addressed.

rier transformation of the reconstructed FID will have the diagonal resonance removed as long as its amplitude is much stronger than the other resonances, which is normally the case in 2D homonuclear spectra. Similarly, diagonal peak suppression can also be achieved by the same procedure on the backward Toeplitz matrix based on the backward linear prediction method (13). When the off-diagonal peaks are not much smaller than the diagonal ones, a larger window size, M , is required to differentiate the singular values corresponding to the off-diagonal and diagonal peaks.

The use of the above algorithm in the t_1 domain for the removal of large diagonal peaks from the signal $S(t_1, f_2)$ obtained after Fourier transformation of a 2D FID $S(t_1, t_2)$ in the t_2 domain requires the following steps: (i) Fourier transformation in the t_2 domain, (ii) phase correction to absorption and discarding of the imaginary part of f_2 , (iii) removal of the larger diagonal peaks in the t_1 domain by the SVD method, (iv) Fourier transformation in the t_1 domain, (v) phase correction to absorption and discarding of the imaginary part of f_1 , (vi) recovery of dispersive part of f_2 via Hilbert transformation, and (vii) phase correction to absorption. 2D spectra obtained in this manner are free from the dispersive diagonal peaks, rendering spectra that can be analyzed easily. Since the method, which works with an arbitrary phase of the 1D FID, is a 1D method applied in the F_1 domain, it is critical to phase the F_2 domain to pure absorption and to discard the dispersive signal in order to effectively remove diagonal peaks.

To illustrate the utility of the proposed procedure, we have applied this method to process a phase-sensitive COSY spectrum of the DNA binding compound 8-phenylmenthanol-4-alkyl-cyclohexyleneacetic ester dissolved in CDCl_3 with a data matrix size of $1024^* \times 256^*$, with $*$ denoting complex number. The phase-sensitive COSY spectrum was recorded on a Varian Inova 500 spectrometer. The undesirable dispersive diagonal peaks shown in the corresponding Fourier transformed spectrum in Fig. 1A makes accurate spectral analysis a formidable task. This difficulty is essentially eliminated as shown in Fig. 1B with the application of the method described above. In Figs. 2A and 2B, the enlarged regions of the phase-sensitive COSY spectra between 7.1 and 7.6 ppm clearly indicate effectiveness of the proposed processing scheme.

The final phase correction in f_2 was achieved by using Hilbert transformation to recover the imaginary part of f_2 and adding a 90° phase correction. The diagonal peaks have largely been removed without loss of the information offered by the off-diagonal peaks. Residual signals left in the spectra are due to multiplet diagonal peak structures and relatively small amplitude and frequency differences between the diagonal and off-diagonal resonances. As can be seen from Figs. 1 and 2, which are plotted at the same contour levels, the incomplete removal of the diagonal peaks causes little interference with the analysis of the processed spectra. The Fou-

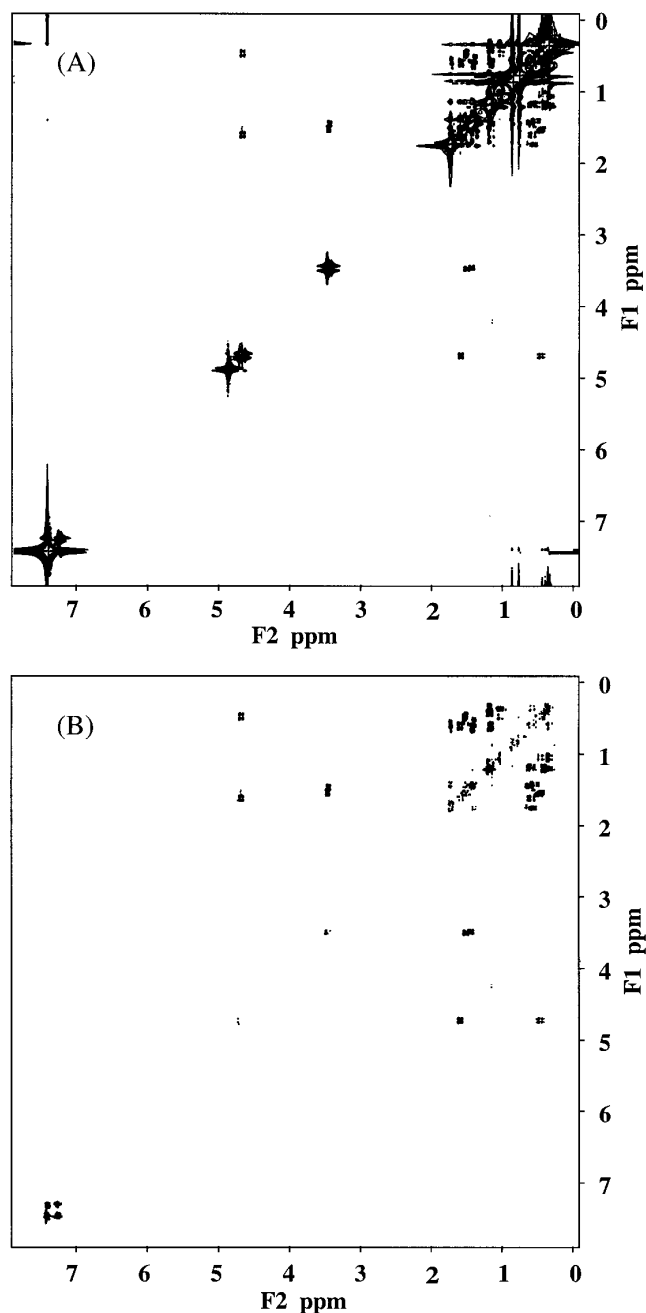


FIG. 1. The Fourier transformed phase-sensitive COSY spectrum of alkyl-cyclohexyleneacetic ester, recorded in CDCl_3 at 300 K on a Varian Inova 500 spectrometer: (A) phased 2D spectrum with large dispersive diagonal peaks, (B) the spectrum processed with the scheme described in the text. The window size used for the processing was 40. The small residual diagonal peaks are due to incomplete peak suppression by the proposed algorithm as explained in the text.

rier and Hilbert transformations and other NMR processing were carried out with the nmrPipe processing package (15).

In conclusion, we have shown that undesirable dispersive peaks on the diagonal of phase-sensitive COSY spectra can

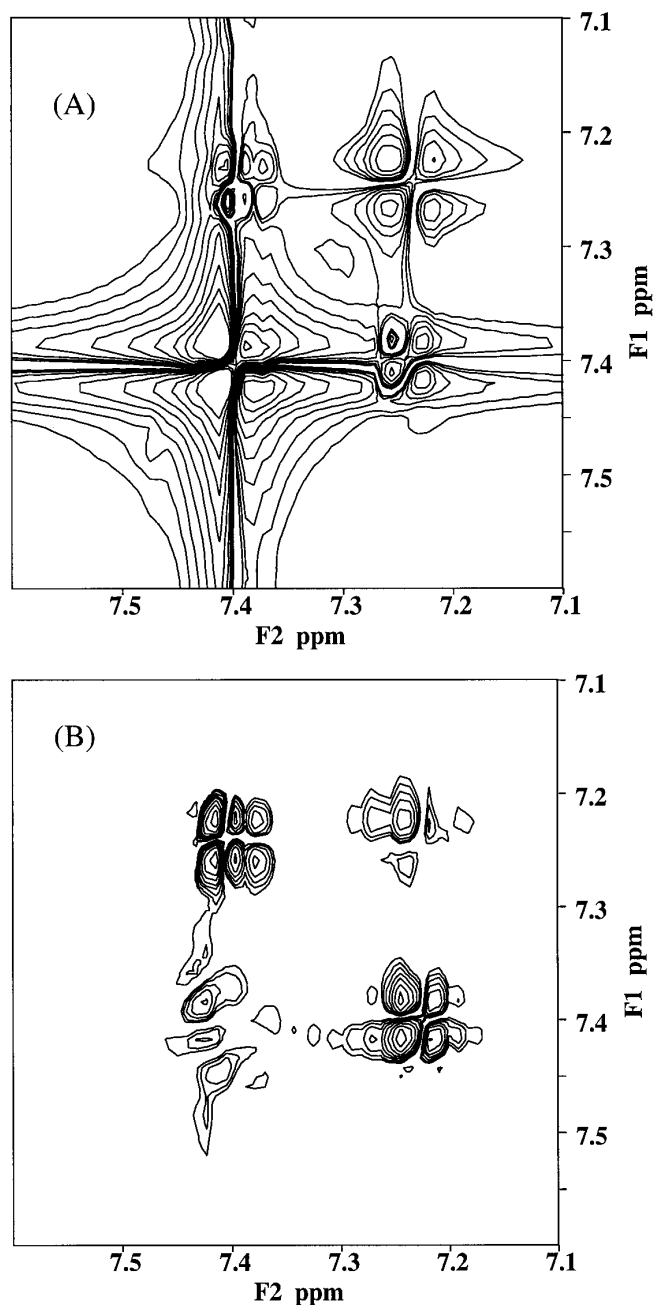


FIG. 2. The enlarged spectral regions of the phase-sensitive COSY spectra before (A) and after (B) applying the proposed processing scheme. The asymmetric off-diagonal peaks are due to the higher spectral resolution in the F_2 domain.

easily be removed by singular value decomposition without loss of the information in the off-diagonal peaks. The proposed method can be applied to remove strong diagonal peaks in NOESY, ROESY, and other correlation spectra which sometime introduce severe spectral distortions, such as t_1 -ridges, making analysis of the spectra difficult. A potential problem with the method occurs when off diagonal peaks are larger in amplitude than or equal to diagonal peaks, such as in DQF-COSY spectra. Off-diagonal peaks which are close to strong diagonal peaks will have different degrees of distortion in the final processed spectrum depending on how close they are to the diagonal peaks. This method can readily be automated and applied to the processing of higher-dimensional NMR spectra.

ACKNOWLEDGMENTS

The work was supported by the Hong Kong Research Grants Council (HKUST563/95M). The authors thank Dr. D. Smith for useful discussions.

REFERENCES

1. J. Jeener, Ampere International Summer School, Basko Polje, Yugoslavia, 1971.
2. W. P. Aue, E. Bartholdi, and R. R. Ernst, *J. Chem. Phys.* **64**, 2229–2246 (1976).
3. N. Muller, R. R. Ernst, and K. Wuthrich, *J. Am. Chem. Soc.* **108**, 6482–6492 (1986).
4. L. Mueller, *J. Magn. Reson.* **72**, 191–196 (1987).
5. D. Marion and A. Bax, *J. Magn. Reson.* **80**, 528–533 (1988).
6. M. S. Friedrichs, W. J. Metzler, and L. Mueller, *J. Magn. Reson.* **95**, 178–183 (1991).
7. D. Marion, M. Ikura, and A. Bax, *J. Magn. Reson.* **84**, 425 (1989).
8. S. Glaser and H. R. Kalbitzer, *J. Magn. Reson.* **68**, 350 (1986).
9. P. Tsang, P. E. Wright, and M. Rance, *J. Magn. Reson.* **88**, 210–215 (1990).
10. I. Pelczer, *J. Am. Chem. Soc.* **113**, 3211–3212 (1991).
11. L. Mistchang, C. Cieslar, T. A. Holak, and H. Oschkinat, *J. Magn. Reson.* **92**, 208–217 (1991).
12. G. Zhu, D. Smith, and Y. Hua, *J. Magn. Reson.* **124**, 286–289 (1997).
13. H. Barkhuijsen, R. De Beer, W. M. M. J. Bovee, and D. Van Ormondt, *J. Magn. Reson.* **62**, 465–481 (1985).
14. G. H. Golub and C. F. Van Loan, "Matrix Computations," Johns Hopkins, Univ. Press, Baltimore, MD (1983).
15. F. Delaglio, S. Grzesiek, G. Vuister, G. Zhu, J. Pfeiffer, and A. Bax, *J. Biomol. NMR* **6**, 277–293 (1995).